

IN THE SPECIFICATION

Please replace paragraph 4 with the following paragraph:

Currently research, therefore, is now focused on modifying the 85-90% screening protocol to lower the 5% false positive rate while maintaining the 85-90% detection efficiency. For example, one approach described in Wald NJ, Watt HC, Hackshaw, AK. N. Engl J Med, 341(7):461-7 (August 12, 1999) suggests measuring levels of screening markers during two stages of pregnancy, *i.e.* during the first and second trimester to determine a patient's risk of having a fetus with Down Syndrome. Although such an approach may reduce the false positive rates of detection, it presents the disadvantage of not providing a result until later in pregnancy. A better approach would be using additional screening markers during the first trimester to maintain the advantages of early detection. Two additional markers that have been suggested are blood flow in the ductus venous and nasal bone identification. Measurement of both of these markers, however, is ~~quite~~ difficult to perform and requires a significant amount of training even for experienced sonographers. In addition, there is some concern about the safety of using color Doppler ultrasound during pregnancy to measure the ductus venosus blood flow.

Please replace paragraph 18 with the following paragraph:

In another implementation of this step of the method of the present invention, this implementation, the relative frequencies of each of the unaffected distribution and the affected distribution are determined by known statistical techniques. For example, the relative frequencies may be determined by a multivariate Gaussian Gaussian distribution. In a multivariate Gaussian Gaussian distribution, the relative frequency of each of the unaffected distribution and the affected distribution of each of the unaffected distribution and the affected distribution can be determined by the following formula:

$$\text{Relative Frequency} = \frac{\exp(-0.5Z^T R^{-1} Z)}{(\prod(\sigma)(2 \times \pi)^{p/2} \det(R)^{1/2})}$$

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where  $p$ = the number of secondary markers;

$\prod(\sigma)$ = the product of the standard deviations for each marker;

$Z$  is vector containing the Z-score of each marker (the patient's marker value - the mean of the marker value from the affected or unaffected pregnancies)/the standard deviation of the marker value from the affected or unaffected pregnancies;

$Z^T$  is the transpose of  $Z$ ;

$R$  is a matrix of the reference data correlation coefficients between the BPD/OFD ratio marker and each secondary marker and between each pair of secondary markers; and

$\det(R)$  is the determinant of the  $R$  matrix.